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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/561,670	12/19/2005	Franco Macchi	207,380	5848

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EXAMINER	
BLAND, LAYLA D	
ART UNIT	PAPER NUMBER
1623	
MAIL DATE	DELIVERY MODE
02/03/2011	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/561,670	MACCHI, FRANCO	
	Examiner	Art Unit	
	LAYLA BLAND	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *1/4/2011*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This office action is a response to Applicant's amendment submitted January 4, 2011.

Claims 7-13 are pending and are examined on the merits herein.

The following rejection of record is maintained:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 7-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Di Schiena (EP 0444492, April 9, 1991, PTO-1449 submitted May 3, 2007) in view of Saxen et al. (Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1997; 84:356-61, of record).

Di Schiena teaches pharmaceutical compositions comprising 0.2 to 10% sodium hyaluronate having molecular weight between 800,000-4,000,000, preferably 1,000,000-2,000,000 [page 2, line 52] for the treatment and prophylaxis of inflammatory affections of the oral cavity [claims 1-10].

Di Schiena does not exemplify the treatment of recurrent oral aphthous ulcers using the composition.

Saxen teaches that recurrent aphthous ulcers are a common disorder, causing pain derived from inflammatory sensitization of nerve endings, and the most common treatment is topical anesthetics and topical steroids for pain management [page 356, first two paragraphs]. Adults having aphthous ulcers were treated with 3% diclofenac in 2.5% hyaluronan, 2.5% hyaluronan, or 3% viscous lidocaine. A 48% reduction in pain was observed 10 minutes after application with no significant difference between the three topical agents [see abstract]. Ulcers were smaller after treatment with HA [page 359, Table 1]. The blunting action of hyaluronan may be due to the coating action over the ulcer [page 360, second full paragraph], and the protective layering of the ulcer was a significant component of the overall treatment effect [page 360, third full paragraph].

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use Di Schiena's composition for the treatment of recurrent aphthous ulcers. Di Schiena teaches that HA of molecular weight 1,000,000-2,000,000 is useful for treating inflammatory affections of the oral cavity, including stomatitis, but does not specifically mention recurrent aphthous ulcers. Saxen teaches that HA alone can be used to treat recurrent aphthous ulcers, resulting in a reduction in pain and smaller ulcers, but is silent with respect to the molecular weight of the HA. The skilled artisan could expect that Di Schiena's composition would be useful for the treatment of a specific inflammatory affection of the oral cavity, recurrent oral aphthous ulcers, because Saxen teaches that HA is effective for treatment of recurrent oral aphthous ulcers. The skilled artisan could expect that HA of molecular weight 1,000,000-2,000,000 could be effectively used in the method taught by Saxen because Di Schiena

teaches that HA of that molecular weight is useful for treatment of inflammatory conditions of the mouth. Thus, the claimed invention is obvious over the prior art.

Response to Arguments

Applicant argues that the 48% reduction in pain refers only to the diclofenac/HA preparation, and that page 359, column 1, line 5 states that neither lidocaine nor hyaluronan were significantly different from baseline pain level. This argument has been carefully considered but is not persuasive. The Saxen abstract clearly states that there was a 48% reduction in pain 10 minutes after application, and that there was no significant difference between the three topical agents at that time. The statement on page 359 refers to the pain level at 1-8 hours after application. Thus, the agents were all effective at 10 minutes after application. Based on Saxen's teachings alone, the skilled artisan would conclude that HA alone is effective for short-term pain relief due to oral aphthous ulcers.

Applicant argues that Saxen's teachings with respect to reduced size and number of lesions after HA administration are not statistically significant and that Saxen states that no significant change was observed. This argument is again acknowledged.

Applicant also argues that the claims are drawn to treatment of oral aphthous ulcers, not treatment of pain due to oral aphthous ulcers. The claims are interpreted to encompass treatment of symptoms. See MPEP 904.02: "During patent examination, the claims are given the broadest reasonable interpretation consistent with the specification." Treatment of symptoms is mentioned repeatedly in the specification, and

so treatment of symptoms is consistent with the specification. Furthermore, DiSchiena that HA is useful as an *active principle* for therapy and prophylaxis of disorders characterized by inflammatory affectations of the oral cavity. DiSchiena also teaches the properties of HA which explain why it is suitable for use as an active principle, including acceleration of tissue repair processes [page 2, lines 22-24]. DiSchiena also teaches that the benefits of HA are *in addition to* its use as a vehicle for promoting absorption of other active agents [page 2, lines 25-28].

Applicant argues that RAS is a pathology of unknown origin, and that different classes of ulcers require different treatments. Saxen teaches that, although the specific cause of RAS remains unknown, a common pathogenic event is a local, cell-mediated inflammatory response. DiSchiena teaches HA for treatment of disorders characterized by inflammatory affectations. Saxen also teaches that adhesion molecules are up-regulated in endothelial cells associated with aphthous ulcers and HA binds to adhesion molecules. Thus, the skilled artisan would conclude that DiSchiena's teachings would be applicable to treatment of RAS.

Applicant argues that Saxen only teaches the use of HA as a vehicle. This argument is not persuasive because, as set forth above, DiSchiena teaches the benefits of HA in addition to its use of a carrier.

Applicant argues that the long-term treatment effects described in Annex 1 are unexpected in view of Saxen's teachings. This argument is not persuasive because DiSchiena teaches that HA can be used as the active principle in treating oral ulcers. Thus, a treatment effect is not unexpected.

For these reasons, the rejection is maintained.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LAYLA BLAND whose telephone number is (571)272-9572. The examiner can normally be reached on Monday - Friday, 7:00 - 3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anna Jiang can be reached on (571) 272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Layla Bland/
Examiner, Art Unit 1623